Amendments to the Claims:

Amendments to and cancellations of claims are made without prejudice or disclaimer. This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1.   (currently amended) A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

providing an ensemble of related backbone structures;

applying a protein design algorithm to generate a protein sequence or set of protein sequences;

sampling and evaluating energetic fitness of one or more amino acids at positions in at least one backbone structure; and

generating a probability matrix for said amino acids that represent a viable sequence space for said ensemble of backbone structures.

2.   (original) A method according to claim 1 further comprising the step of:
 generating a single protein sequence from said probability matrix.

3.   (previously presented) A method according to claim 1 further comprising the step of: producing a combinatorial library of proteins from said probability matrix.

4.   (original) A method according to claim 1 wherein said steps are repeated more than once to generate said probability matrix

5.   (original) A method according to claim 1 wherein said protein design algorithm comprises an optimization procedure selected from the group of: dead end elimination algorithm; genetic algorithm; Monte Carlo algorithm; and self consistent mean field theory algorithm or combinations thereof.

6.   (previously presented) A method according to claim 1 wherein at least one backbone structure of the ensemble is derived from the structure of a natural protein.

7.   (previously presented) A method according to claim 1 wherein at least one backbone structure of the ensemble is generated by comparative modeling.

8-13.   (cancelled)

14.   (previously presented) A method according to claim 1 wherein said ensemble of related backbone structures comprises backbone structures of a family of natural proteins.

15.   (withdrawn) A method according to claim 1 wherein said ensemble of related backbone structures is derived from an NMR structure.

16.   (previously presented) A method according to claim 1 wherein said ensemble of related protein backbone structures is generated by a Monte Carlo simulation.

17.   (withdrawn) A method according to claim 1 wherein said ensemble of related protein backbone structures is generated by a molecular dynamics simulation.

18.   (previously presented) A method according to claim 1 wherein the information from at least two probability matrices is combined to satisfy at least two constraints on sequence space.

19 - 37. (cancelled)

38. (currently amended) A method according claim [[25]] 2 wherein the amino acid sequence of the single protein sequence is selected by identifying the amino acid with the lowest free energy at each position.

39. (currently amended) A method according claim [[26]] 65 further comprising selecting an upper limit on free energy, allowing amino acid variations among amino acids that are below the upper free energy limit, to thereby identify and generating and synthesizing a library of protein sequences from said probability matrix.

40. (currently amended) A method according claim [[26]] 65 further comprising incorporating amino acids at incrementally lower probabilities until a desired complexity is achieved, thereby identifying and generating and synthesizing a library of protein sequences from said probability matrix.

41. (currently amended) A method according to claim [[8]] 18 wherein the at least two constraints comprise a first constraint corresponding to a first structural form and second constraint corresponding to a second structural form that is distinct from the first structural form.

42. (currently amended) A method according to claim [[8]] 18 wherein a first and second probability matrix the at least two probability matrices are combined by adding or subtracting free energies values from said probability matrices.

43. (currently amended) A method according to claim [[8]] 18 wherein the combining process is iterated.

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44.   (previously presented) The method of claim 1 wherein the sampling an amino acid position comprises freezing side chain identities and rotamers at positions in the protein other than the sampled amino acid position.

45.   (previously presented) The method of claim 1 wherein the probability matrix is expressed as a set of partition functions.

46.   (previously presented) The method of claim 1 wherein the probability matrix is expressed as a free energy value.

47.   (previously presented) The method of claim 1 wherein the probability matrix comprises information for all twenty amino acids.

48.   (currently amended) The method of claim 3 further comprising screening or selecting one or more proteins from the library for a desired property.

49.   (previously presented) The method of claim 4 wherein, in a subsequent cycle, the protein design algorithm uses the probability matrix from a previous cycle.

50.   (currently amended) The method of claim 48 wherein the screening or selecting comprises identifying a protein with enhanced catalytic activity, improved thermodynamic stability, or altered specificity, relative to an initial protein whose backbone structure is one of the backbone structures of the ensemble.

51-59. (cancelled)

60. (previously presented) A method of providing a protein, the method comprising:

performing the method of claim 1; and

producing at least one protein comprising a sequence based on said probability matrix.

61. (previously presented) A method of providing a protein library, the method comprising:

performing the method of claim 1; and

producing a library of proteins that include proteins that each comprise a sequence based on said probability matrix.

62- 64. (cancelled)

65. (currently amended) A method executed by a computer under the control of a program, said computer including a memory for storing the program, the method comprising:

providing an ensemble of related backbone structures;

applying a protein design algorithm to generate a protein sequence or set of protein sequences; and

generating a matrix of amino acid probabilities that represents a viable sequence space for said ensemble of backbone structures.

66. (cancelled)

67. (previously presented) The method of claim 1 wherein the step of sampling and evaluating fitness of one or more amino acids comprises sampling and evaluating fitness of different rotamers of the one or more amino acids at position in at least one backbone structure.

68.   (currently amended) The method of claim [[3]] 2 further comprising producing a protein that comprises the single protein sequence.